

## Prevalence of Metabolic Syndrome in Patients with Lichen Planus: A Cross-sectional Study from a Tertiary Care Center

### Abstract

**Background:** There have been reports of association between lichen planus (LP) and metabolic syndrome and its various parameters. **Aims and Objectives:** To determine the prevalence of metabolic syndrome in patients with LP and to determine the association between the morphologic types of LP and metabolic syndrome. **Materials and Methods:** In this cross-sectional study conducted over a period of 1 year, 70 clinically diagnosed patients with LP were included and evaluated for metabolic syndrome based on the modified National Cholesterol Education Program: Adult Treatment Panel III guidelines. Data were analyzed using Statistical Package for the Social Sciences version 17 software, and inferential statistical tools such as *t*-test for continuous data and Chi-square test for categorical data were used. **Results:** A 35.7% prevalence of metabolic syndrome was found in patients with LP. The average duration of LP was found to be higher in patients with metabolic syndrome. There was a higher prevalence of central obesity, increased fasting blood sugar, and low high-density lipoprotein-cholesterol in patients with LP. **Conclusion:** Metabolic syndrome was seen in 25 patients (35.7%) with LP. It is important to advise our patients to adopt healthy lifestyle choices to help prevent comorbidities and improve the general health of population. As this study was a cross-sectional study, the directionality of the association between LP and metabolic syndrome could not be assessed. Lack of controls and a small sample size are other limitations of our study.

**Keywords:** Lichen planus, metabolic syndrome, obesity

### Introduction

Lichen planus (LP) has been associated with metabolic disorders such as dyslipidemia and diabetes mellitus.<sup>[1,2]</sup> Antioxidant defense mechanisms are significantly altered in LP causing an increase in oxidative damage to lipids, protein, and DNA, which may be involved in inflammatory processes of the disease.<sup>[3]</sup> Epidermal cells in LP have shown abnormalities in enzymatic activity and defective carbohydrate expression.<sup>[4]</sup> As a relatively common immune-mediated disorder, LP may serve as an external indicator of underlying immune and metabolic dysfunction. This study was intended to find prevalence of metabolic syndrome in patients with LP.

### Materials and Methods

This was a cross-sectional study conducted over a period of 1 year from January to December 2015, to determine the prevalence of metabolic syndrome in LP,

in patients attending outpatient department of a tertiary care center in north Kerala. All clinically diagnosed patients with LP with age >18 years who were willing to give written informed consent to participate in the study were included. Patients who were on treatment with systemic steroids, retinoids, or ciclosporin for the past 1 month were excluded. The study was approved by the institutional ethics and research committee.

Data were collected from all the patients in a pretested structured questionnaire and the data were analyzed using appropriate statistical software. Body mass index (BMI) was calculated as weight (kg)/height (m<sup>2</sup>). Waist circumference was measured using a measuring tape which was horizontally applied over the uppermost part of the hip bone and tape was snug without causing undue compressions on the skin. Venous blood samples were taken at enrolment visit after the subjects had fasted overnight. Serum high-density lipoprotein

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(HDL)-cholesterol (HDL-C) and triglycerides (TG) were measured with enzymatic procedures. Plasma glucose was measured using hexokinase method. Metabolic syndrome was identified in the presence of three or more criteria of the modified National Cholesterol Education Program: Adult Treatment Panel III (NCEP-ATP III) guidelines [Table 1].<sup>[5]</sup>

For NCEP criteria, abdominal obesity is a component of the syndrome but not a prerequisite for its diagnosis, in contrast to International Diabetes Federation criteria. According to Lee *et al.*,<sup>[6]</sup> the definition of metabolic syndrome should have central obesity as an optional rather than essential criterion as this would identify more high-risk individuals among the Asians.

### Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences version 17 software. Descriptive statistical tools such as mean and standard deviation for continuous data, frequencies and percentage for categorical data, and inferential statistical tools such as *t*-test for continuous data and Chi-square test for categorical data were used.  $P < 0.05$  was considered significant.

### Results

Of the 70 patients enrolled, 33 (47.1%) were males and 37 (52.9%) were females with a male-to-female ratio of 1:1.12. The mean age of the patients were  $50.6 \pm 13.2$  years. The mean age of onset of LP was  $48.8 \pm 13.5$  years. The average duration of LP in months was  $20.5 \pm 26.1$ . Among the patients enrolled in the study, 81.4% had skin LP, 55.7% had oral LP, 37.1% had both skin and oral involvement, and 2.9% had genital LP.

The most common morphologic type of skin LP was classic LP in 45 patients (78.9%). LP pigmentosus and eruptive LP constituted 12.3% of skin LP, whereas 5 (8.8%) had hypertrophic LP. The most common oral LP morphology

in this study was reticular in 27 (69.2%) followed by plaque-like in 10 (25.7%) and erosive in 2 patients (5.1%). Food especially hot and spicy food as an aggravating factor was found in 85.7% of patients with oral LP. Stress was found to aggravate LP in 87.5% patients with Cutaneous involvement and in 46.9% patients with oral involvement.

A total of 25 patients (35.7%) enrolled in this study were found to have metabolic syndrome, of which 17 (68%) were females and 8 (32%) were males. About 31.6% among patients with skin LP, 43.6% among patients with oral LP, and 38.5% patients with both skin and oral involvement had metabolic syndrome, but none of the values was statistically significant ( $P$  values 0.131, 0.123, and 0.712, respectively).

In patients with cutaneous LP with metabolic syndrome, 16 patients (88.9%) had classic LP and 11.1% had eruptive LP. Among patients with oral LP with metabolic syndrome, 76.5% had reticular type, 11.8% had erosive, and 11.8% plaque-like oral LP. There were two patients with eruptive skin LP and two patients with erosive oral LP and all these four had metabolic syndrome [Figure 1].

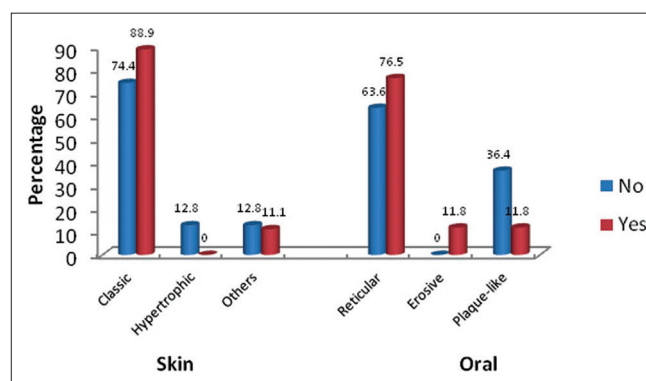
It was noted that the maximum number of patients with metabolic syndrome was in the age group of 51–60 years. The average duration of LP in patients with metabolic syndrome was 21.52 months and in those without metabolic syndrome was 19.84 months [Figure 2]. Among patients who had experienced relapse of LP, 29.4% had metabolic syndrome ( $P$  value 0.533).

Among various metabolic syndrome parameters, central obesity was found in 32 (86.5%) female patients and 9 (27.3%) male patients, hypertension (HT) was present in 13 (18.6%) patients, elevated fasting blood glucose in 38 (54.3%), hyper triglyceridemia in 24 (34.3%), and decreased HDL-cholesterol in 21 (56.8%) females and 12 (36.4%) males in the study population [Figure 3].

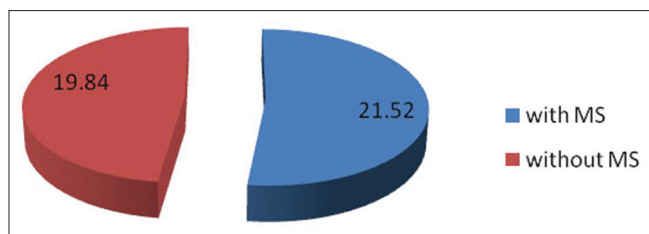
Increased fasting blood sugar (FBS) was noted in 52.6% patients with cutaneous LP, 59% patients with oral LP; but no significant statistical correlation was noted between patients with normal and increased FBS in the two groups.

**Table 1: Modified National Cholesterol Education Program: Adult Treatment Panel III criteria for clinical diagnosis of metabolic syndrome**

Central obesity	Waist circumference
	≥90 cm in males
	≥80 cm in females
Hypertension	Blood pressure
	≥130 mm Hg systolic or
	≥85 mm Hg diastolic or
	Specific medications
Fasting plasma glucose	≥100 mg/dl or specific medications
Hyper triglyceridemia	Triglyceride ≥150 mg/dl or
	specific medications
Low HDL cholesterol	≤40 mg/dl in males
	≤50 mg/dl in females or
	Specific medications



**Figure 1: Comparison of morphology of lichen planus based on metabolic syndrome**



**Figure 2: Average duration of lichen planus (months) based on metabolic syndrome**

The majority of female patients with skin LP and oral LP showed low HDL-cholesterol level, but it was found to be normal in most of the male patients. It was noted that 17.5% patients with cutaneous LP and 15.4% patients with oral LP had HT, and 33.3% patients with cutaneous LP and 43.6% patients with oral LP had hyper triglyceridemia. None of the latter three parameters had significant *P* value compared with their normal counterparts.

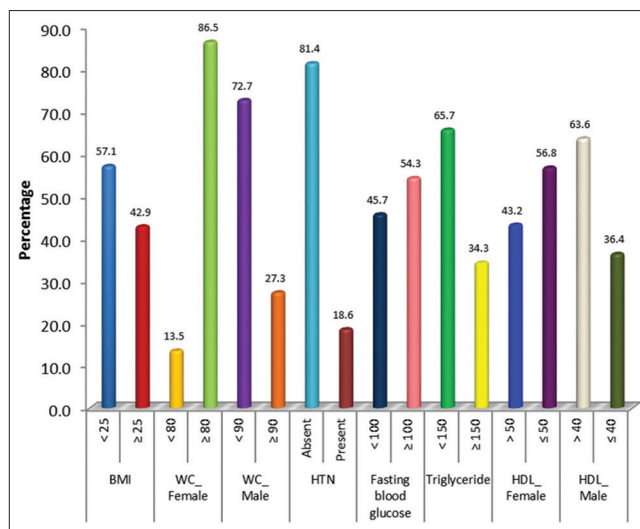
The mean BMI of patients with LP in the study was 24.26 kg/m<sup>2</sup>. Around 42.9% of patients were found to have BMI  $\geq 25$  kg/m<sup>2</sup>. Among patients with metabolic syndrome, 60% (*n* = 15) were overweight (BMI: 25–29.9 kg/m<sup>2</sup>). Two patients in this study were found to be obese (BMI  $\geq 30$  kg/m<sup>2</sup>) and both had metabolic syndrome. Among patients without metabolic syndrome, 28.8% (*n* = 13) were overweight and none was obese.

Family history of LP was present in six patients. Among them, the duration of disease ranged from 3 months to 4 years, with a mean duration of 22.3 months. On comparing family history parameters such as diabetes mellitus (DM), HT, dyslipidemia, and coronary heart disease (CAD) in patients with and without metabolic syndrome, it was noted that there was a significant association between family history of HT and DM with metabolic syndrome with *P* values 0.035 and 0.049, respectively.

## Discussion

LP is an immune-mediated disease and antigens are processed by Langerhans cells and then presented to T lymphocytes. Several cytokines such as TNF- $\alpha$ , IL-6, IL-10, and IL-4 are involved in pathogenesis of LP which explains its association with lipid metabolism disturbances such as increased serum TG and decreased HDL-cholesterol, which in turn increases cardiovascular risk.<sup>[2]</sup> As a common inflammatory disorder affecting 0.22%–5% of population worldwide, LP may serve as an external indicator of underlying immune and metabolic dysfunction.<sup>[7]</sup>

Females outnumbered males in our study, with male-to-female ratio being 1:1.12. The mean age of patients with LP in years was  $50.6 \pm 13.2$ . The mean age of onset of LP in the study population was found to be  $48.8 \pm 13.5$  years. The most common morphologic type of skin LP was classic and that of oral LP was reticular; similar findings were reported in previous studies.<sup>[8,9]</sup>



**Figure 3: Distribution of body mass index and metabolic syndrome parameters in patients with lichen planus**

The prevalence of metabolic syndrome in different parts of India ranges from 11% to 41%, with a study conducted in urban population from South India reporting a prevalence of 27%, with 26.4% in males and 28.1% in females.<sup>[10,11]</sup> In this study, 35.7% had metabolic syndrome of which 68% were females and 32% were males. Metabolic syndrome was found in 31.6% patients with skin LP and in 43.6% with oral LP; among these, 38.5% patients had both skin and oral involvement; but none of these was statistically significant.

Arias-Santiago *et al.* reported a higher prevalence of metabolic syndrome in patients with LP (30% males and 24% females) compared with controls, but this was not statistically significant.<sup>[12]</sup> Baykal *et al.* reported a significantly higher prevalence of metabolic syndrome in patient with mucosal LP.<sup>[13]</sup> A recent study by Krishnamoorthy *et al.* reported a higher prevalence of metabolic syndrome in patients with oral LP.<sup>[14]</sup> In a study by Kurian *et al.* among 40 patients with LP, 18 (45%) patients had metabolic syndrome when compared with 32 (40%) individuals without LP.<sup>[15]</sup> Another Indian study also found that total cholesterol, TG, HDL-C, LDL-C, and FBS values were significantly higher in LP cases than in controls.<sup>[4]</sup> ATP-III criteria for metabolic syndrome were met by 6% of the patients with LP versus 2% of the controls in a study by Vidya *et al.*<sup>[16]</sup> [Table 2].

It was noted that among patients with skin LP with metabolic syndrome, 88.9% had classic LP, and among patients with oral LP with metabolic syndrome, 76.5% had reticular type. This could be because of higher prevalence of these morphologic types. In this study, there were two patients with eruptive skin LP and two with erosive oral LP, and all the four had metabolic syndrome. A study by Lopez-Jornet *et al.* reported significantly higher triglyceride levels in patients with atropho-erosive type of oral LP than



**Table 2: Comparison of metabolic syndrome in LP in previous studies**

Authors	Year	Metabolic syndrome (%)
Santiago <i>et al.</i> <sup>[12]</sup>	2011	27
Krishnamoorthy <i>et al.</i> <sup>[14]</sup>	2014	27
Bayal <i>et al.</i> <sup>[13]</sup>	2015	26
Vidya <i>et al.</i> <sup>[16]</sup>	2016	6
Kurian <i>et al.</i> <sup>[15]</sup>	2017	45

reticular-papular type.<sup>[17]</sup> Increased levels of S cholesterol and LDL-C were seen in patients with oral LP when compared with normal healthy individuals in a study by Krishnamoorthy *et al.* as well.<sup>[14]</sup>

Baykal *et al.* reported longer duration of LP in patients with insulin resistance, which is a central feature of metabolic syndrome.<sup>[13]</sup> In this study too it was found that the average duration of LP in patients with metabolic syndrome was slightly higher than in those without metabolic syndrome.

Increased values of waist circumference as a measure of central obesity were found in 86.5% of female patients and 27.3% of male patients with LP in our study. Increased waist circumference was seen in 45.45% of female patients with LP compared with 14.29% of male patients with LP in another study as well.<sup>[16]</sup> The presence of increased abdominal girth and low HDL values were significantly more among females, whereas increased TG level was more among males in general population in a study by Roshni as well.<sup>[11]</sup> As increased waist circumference is an easily measurable parameter, it may be taken as an indicator for the occurrence of metabolic syndrome in patients with LP.

Among other metabolic syndrome parameters, it was noted that HT was present in 18.6% patients, elevated fasting blood glucose in 54.3%, hyper triglyceridemia in 34.3%, and decreased HDL-cholesterol in 56.8% females and 36.4% males. Arias-Santiago *et al.* reported a significant higher prevalence of hyper triglyceridemia and decreased HDL-cholesterol in patients with LP.<sup>[12]</sup> Cohen *et al.* also reported a significant higher prevalence of dyslipidemia in LP.<sup>[1]</sup> Higher values of TG and low levels of HDL-cholesterol were associated with transition from atheroma to athero thrombosis and thereby increased cardiovascular risk.<sup>[12]</sup> Polic *et al.* have shown that dietary regulation of the imbalanced concentrations of serum lipids leads to improvement in clinical signs of LP, thus confirming the connection between dyslipidemia and LP.<sup>[18]</sup>

Baykal *et al.* found that among the various metabolic syndrome parameters, fasting blood glucose and diastolic blood pressure were seen to be significantly higher in patients with LP.<sup>[13]</sup> Increased FBS was noted among 52.6% patients with skin LP and 59% patients with oral LP; but there was no statistical significance. The association between oral LP and diabetes was first reported by Grispan

*et al.* in 1963.<sup>[19]</sup> Romero *et al.* and Lopez-Jornet *et al.* reported a higher prevalence of DM in oral LP.<sup>[2,17]</sup>

The majority of female patients in this study had low HDL-cholesterol level, but it was found to be normal in most of the male patients. Higher prevalence of dyslipidemia in female patients with LP was reported by Cohen *et al.*<sup>[3]</sup> However in contrast to this study, a significantly lower HDL-cholesterol values were reported in male patients with oral LP in a case-control study by Lopez-Jornet *et al.*<sup>[17]</sup>

It was observed in various studies that most of the obese people (BMI  $\geq 30$  kg/m<sup>2</sup>) have relatively low insulin sensitivity, and that insulin resistance occurs even with BMI 25 kg/m<sup>2</sup> in some South Asian population.<sup>[20,21]</sup> The mean BMI of patients with LP in this study was 24.26 kg/m<sup>2</sup>. This was slightly lower than that observed by Arias-Santiago *et al.* in patients with LP (26.4 kg/m<sup>2</sup>).<sup>[12]</sup> In our study, it was found that 42.9% patients were overweight (BMI: 25–29.9 kg/m<sup>2</sup>). Among patients with metabolic syndrome, 60% ( $n = 15$ ) were overweight and 8% ( $n = 2$ ) were obese (BMI  $\geq 30$  kg/m<sup>2</sup>), whereas in patients without metabolic syndrome only 28.8% ( $n = 13$ ) were overweight and none was obese. As increasing BMI puts the patients at risk of metabolic syndrome, curbing obesity is an important aspect of reducing the incidence of metabolic syndrome and its complications.

In our study, we compared family history of DM, HT, dyslipidemia, and CAD in patients with and without metabolic syndrome, and significant association was found between family history of HT and DM with metabolic syndrome. As this study was a cross-sectional study, the directionality of the association between LP and metabolic syndrome could not be assessed. Lack of controls is a drawback of our study. Another limitation of our study was small sample size, which resulted in a very few statistically significant correlation in our study. Therefore, we recommend case-control studies with larger sample size to determine any direct association between LP and metabolic syndrome.

The knowledge about the pathogenesis of LP and various cytokines involved could potentially explain the link between LP and metabolic syndrome and its various components. The presence of metabolic syndrome and its components markedly increase the risk of cardiovascular events. Therefore, it is important to advise our patients to adopt healthy lifestyle choices as an easy first step to help prevent comorbidities and improve the general health of population.

## Conclusion

A 35.7% prevalence of metabolic syndrome was found in patients with LP. Central obesity, increased FBS, and low HDL-cholesterol were the metabolic syndrome parameters found to be more common in patients with LP in our study.

As increased waist circumference is an easily measurable parameter, it may be taken as an indicator for the occurrence of metabolic syndrome in patients with LP and a guide to look for the presence of other components of metabolic syndrome. Chronic inflammation in patients with LP might explain its association with metabolic syndrome and its various components. Screening of patients with LP for metabolic syndrome might be useful in detecting individuals at risk and initiating preventive measures to protect against the development of cardiovascular disorders later in life.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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